EXHIBIT A117

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Cancer incidence among women and girls environmentally and occupationally exposed to blue asbestos at Wittenoom, Western Australia

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The impact of crocidolite exposure on the health of former Wittenoom miners and millers (largely male) has been well documented. Less is known about the health outcomes of the 2,968 women and girls who lived ($N = 2{,}552$) and worked ($N = 416$) in the blue asbestos milling and mining town of Wittenoom between 1943 and 1992. Quantitative exposure measurements were derived from dust studies undertaken over the lifetime of the mine and mill and the township. Incident cancers were obtained from the Western Australian (WA) Cancer Registry and the National Cancer Clearing House. Standardized incidence ratios (SIRS) compared Wittenoom females with the WA female population. Exposure-response relationships were examined using a matched case-control study design. There were (47) mesothelioma and (55) lung cancer cases among the 437 cancers in the Wittenoom females over the period 1960–2005. When compared to the WA female population, Wittenoom women and girls had higher rates of mesothelioma and possibly lung cancer. Mesothelioma incidence rates are increasing with the incidence rate of 193 per 100,000 in the period 2000–2005 being more than double that for the period 1995–1999 at 84 per 100,000. A significant exposure-response relationship was present for mesothelioma, but not for lung cancer. Forty years after the asbestos mine and mill at Wittenoom were closed, there is a high toll from cancer among the former female residents of the town and company workers.

Key words: women; cancer incidence; asbestos

The impact of crocidolite exposure on the morbidity and mortality of Wittenoom miners and millers (largely male) has been well documented.[1–3] Less is known about the impact of exposure on the health outcomes of the 3000 women and girls of Wittenoom, who comprised both asbestos workers employed by the Australian Blue Asbestos Company (ABA), and former residents of the Wittenoom township who were not employed directly in the asbestos industry.

This study was undertaken because the results from studies of men may not be pertinent or adequate to characterize the risks among women[4] and cannot be used to examine breast or gynecological cancers. There may also be gender specific responses to asbestos exposure that cannot be determined solely through an examination of male subjects. Susceptibility and carcinogenicity may vary by gender, and the nature and patterns of exposure to asbestos may differ by gender.

Most studies examining asbestos exposure and health outcomes among women have confined their attention to mortality rather than incidence of cancer. This appears most appropriate where the period between diagnosis and death is relatively short (e.g., for malignant mesothelioma and lung cancer), but it relies on the accuracy of cause of death recording and coding which may be contentious for malignant mesothelioma.[5–8] These earlier studies examining cancer mortality and asbestos exposure in women have reported excess mortality from lung and respiratory cancers and malignant mesothelioma. There has been some suggestion that ovarian cancers are also in excess but small numbers make interpretation difficult.[6,7,9]

The women of Wittenoom have been exposed virtually exclusively to crocidolite and quantitative measures of their exposure have been estimated.[2,10] Their sources of asbestos exposure were mixed; for some it was occupational whilst for others it was from the general environment and from the domestic environment in the home where ABA workers' clothes were worn and washed. The aim of this article is to examine cancer incidence in the Wittenoom women, compare it with the Western Australian (WA) female population and examine exposure–response relationships.

Methods

Blue asbestos was mined and milled at Wittenoom Gorge in WA between 1936 and 1966. The township of Wittenoom that developed as a result of the mine and mill was initially located in Wittenoom Gorge, 1 km away from the mine. As the population grew it moved to the flats of the Fortescue River, 12 km from the mine. The State and Commonwealth governments actively encouraged the development of Wittenoom and provided housing for the ABA workers and their families and various township amenities. Asbestos tailings from the mine were distributed throughout the town: on roads and footpaths; on the school playgrounds; on the racecourse; and in the back yards of houses, in an attempt to minimize the fine, irritating dust rising from the red sandy dirt.[10,11] A chronology of events that occurred at Wittenoom is presented in Table I.

Wittenoom workers' and residents' cohorts

Establishment of the Wittenoom workers cohort has been described elsewhere.[2] Briefly, crocidolite (blue asbestos) was mined at Wittenoom gorge in Western Australia from 1936 until 1966. From 1943 until 1966 the principal leases were mined by a single company, ABA which employed over 6,000 people, mostly for short periods (Table I). From employment records a cohort of 6,493 males and 416 (6%) female employees was assembled. Most of the women who worked for ABA were not employed in mining or milling roles but instead worked in the company shop, hotel or offices. When the cohort was assembled vital status was determined for 73.2% of men and 58.0% of the women.[2] To the end of 2000 the vital status of more than 70% of the former female workers was known.

A further cohort were identified from various sources as being former residents of the township of Wittenoom.[11,13] These sources and the percent of people they identified included: state primary school records (22%), admission and out-patient records from the Wittenoom hospital and General Practitioner (20%), the State Electoral Roll for the Pilbara district (12%) questionnaires sent to ABA workers (14%), participants of a cancer prevention program

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TABLE I – CHRONOLOGY OF EVENTS[1] THAT OCCURRED AT WITTENOOM, WESTERN AUSTRALIA

1936	Crocidolite deposits "discovered" and pick and shovel mining commenced
1943	Australian blue asbestos company takes over the principal leases
1946	Establishment of residential settlement in Wittenoom Gorge about 1km downstream from mine and mill
1946	Mines Department Inspector describes dust conditions at Wittenoom as 'terrific'.
1947	Building of town of Wittenoom at entrance to Wittenoom Gorge commenced, 10km from the mine and mill
1948	Town named Wittenoom
1948–1951	Dust levels in mine and mill regularly monitored at 6–8 times "safe" levels.
1950	Wittenoom has 150 houses and population over 500
1958	New "cleaner" mill opens
1960	First mesothelioma case in a worker diagnosed.
1965	Local council warned that the tonnes of asbestos tailings spread around the town could even threaten tourists.
1966	October 8th. Air sampling program using long running thermal precipitators commenced
1966	December 1st. Asbestos mine and mill closes due to economic reasons. Population declines rapidly
1978	November. Government decides to phase out the town of Wittenoom.
1980–83	Some Wittenoom streets closed
1985	December 18th. primary school closed
1992	Government owned buildings demolished and new residents discouraged

[1]Taken from the report of the select committee appointed to inquire into Wittenoom.[12]

and associated publicity (18%) and Wittenoom birth records (4%). Other sources included records from the Catholic Church, Wittenoom burial records, employment lists from the school, hotel, police, hospital and banks and information from the Asbestos Diseases Society of WA (10%). In total 18,553 records collected identifying 5,097 individuals not employed directly in asbestos mining or milling.[10,11]

Between 1991 and 1993 a questionnaire was sent to all former residents of Wittenoom traced to an address in Australia, (N = 3,244, 64%), excepting those participating in a cancer prevention program (N = 641, 13%) from whom the information had already been collected. Date, length and place of residence at Wittenoom, occupation at Wittenoom, whether lived with an asbestos worker or washed the clothes of an asbestos worker, smoking and past medical history as well as demographic information were collected.[14]

After consideration of questionnaire responses, 438 subjects were deleted from the cohort for various reasons; denied living at Wittenoom (n = 209, 48%), no details on date of birth or duration of residence (n = 152, 35%), lived at Wittenoom for less than one month (n = 22, 5%) and 55 (12%) were duplicate records.[14] Therefore follow up status at the end of 1993 was; 2,173 (47%) returned a questionnaire, 641 (14%) were participating in the cancer prevention program, 51 (1%) had permanently departed Australia, 460 (10%) were dead, 785 (17%) had not returned a questionnaire and 549 (11%) were not traced since leaving Wittenoom.[13] Where the person remained untraced, did not return a questionnaire or was dead: if they were related to an ABA worker, then dates and place of residence were assumed identical to that of the worker. For those unrelated to an ABA worker, dates of residence were assumed the same as other family members provided that at least one family member had known exposure. Dates of residence were taken as those found on the various sources used to establish the cohort for all other residents.[10,13] If the untraced person was the wife of an ABA worker and known to have lived with that worker, it was assumed that she washed his clothes. The residents' cohort was considered complete when comparisons between it and the population of Wittenoom recorded at various census dates showed a close correspondence.[11]

Work has continued on the development of this cohort since 1993 and this accounts for differences in the number of persons from those earlier articles.[10,11,13] To the end of 2000 there were 2,608 women and 2,160 men in the residents' cohort.[15]

Women at Wittenoom

All women from both cohorts without a death record and who were not attending a cancer prevention program,[16] were searched for in the Marriage Register of WA to determine if a change of surname had occurred. The search commenced from the year they were last known to be alive. Death certificates of any spouse or birth, death and marriage certificates of children were sought in an attempt to obtain the wife or mothers' maiden name and date of birth. From this search we obtained authenticating information for 235 women previously thought lost to follow up. Fifty six women were excluded because they had insufficient identifying information (missing date of birth, first name etc.) or because they were residents of Wittenoom for less than 1 month. The final cohort therefore consisted of 2,968 women, 416 former workers and 2,552 former residents. As at the end of 2004, 556 women (19%) were known to have died, 1,762 women (59%) were alive and 650 women (22%) were lost to follow up. Women were defined as lost to follow up if there was no "passive" contact since 1999 and were not known to be dead.

Case ascertainment

The cohort was linked to the WA Cancer Registry, to ascertain incident cancers from 1982 to December 2005. Cancers diagnosed prior to 1982 were obtained by manually searching printed computer records of all cancer registrations in Western Australia, as well as searches of hospital admission records at all public hospitals in Australia. Pathologists throughout Australia, and other state and territory cancer registries were sent a list of names of all cohort members and asked to search their records. Completeness of cancer registrations for cancers other than mesothelioma before 1982 are not known, therefore any cancer diagnosed before that period have not been included in the standardized incidence ratios (SIR). The WA Mesothelioma Registry, which assesses and verifies all cases of mesothelioma diagnosed in the state, was established in 1960.[17] Incident cancers among women not resident in Western Australia were obtained from each state and territory Cancer Registry *via* the National Cancer Clearing House, and mesotheliomas from the Australian Mesothelioma Register.[18] The end of follow-up for each state and territory were: Tasmania and South Australia 1999, Northern Territory 1998, Australian Capital Territory, New South Wales, Queensland and Victoria 1997. Cancers were defined using the International Classification of Diseases for Oncology, Second Edition.[19] Data quality checks at the cancer registries are carried out on a continual basis. Pathology coding and entry into database are checked by a second staff member and unusual cases are flagged according to the International Agency for Research into Cancer (IARC's) "Check" routine. Completeness is ascertained by comparisons with reports from radiation oncologists and the hospital morbidity data system which records all details of hospitalizations in Western Australia.[17]

Asbestos exposure assessment

The Mines Department of WA conducted several surveys of dust exposure in the mine and mill between 1948 and 1958 measuring the concentration of particles per cubic centimetre using a koniometer. The upper measurement limit of 1,000 cm^3 was often exceeded and anecdotal evidence suggests that operations were shut down before the inspections commenced. In 1966 airborne

respirable fibers greater than 5 μm in length were measured in various workplaces in the mine and mill and in the township using a Casella long running thermal precipitator.[20] Fiber concentrations ranged from 100 fibers/ml (f/ml) in the bagging room down to 20 f/ml in the mine. Cumulative exposure, measured in fiber per ml years (f/ml years) was calculated for each former worker by adding over all his/her jobs the product of his/her estimated fiber concentration (derived from the dust surveys) and the length of time spent in each job obtained from the ABA employment records.[2] An additional amount was added to the workers exposures reflecting 16 more hours of residential exposure each day and a two day weekend.

In 1973 personal and fixed positional monitors were used to measure environmental levels in the township, and further measurements were taken in 1977, 1978, 1980, 1984, 1986 and 1992.[10] On the basis of these measures residents not working directly with asbestos were assigned an intensity of exposure of 1.0 fiber/ml of air from 1943 to 1957, when an old "dirty" mill was in operation and then 0.5 f/ml from1958 when a new "cleaner" mill was in operation until the time that the mine and mill closed in 1966 (Table I).[10,13] Interpolation between the dust surveys that used personal monitors allocated exposures from 0.5 f/ml in 1966 to 0.010 f/ml in 1992. The township of Wittenoom did not close with the demise of the asbestos mining and milling operation, although there was a significant decline in population at that time.[15] The State Government began to phase out the town from 1992 when some of the buildings were demolished and services withdrawn (Table I). Duration of residence was combined with intensity of exposure to provide a measure of cumulative exposure. Cumulative exposure was then adjusted by a factor of 4.2 to account for 24 hr a day/7 day a week exposure.

The estimates of asbestos exposure have been validated internally by showing an agreement with lung fiber burdens[21] and a clear relationship between all asbestos-related diseases and exposure-response has been repeatedly documented in the cohort.[2,22–24] Further, Hodgson and Darnton, found Wittenoom exposures comparable to exposures reported from other crocidolite mines and found the Wittenoom lung cancer risk (R_L) similar to that from other studies.[25]

Analysis

SIRs were calculated as the ratio of the observed cancers to expected cancers. Confidence intervals were assessed by treating the observed number as a Poisson count with expectation equal to the particular expected numbers. Expected numbers of cancers were estimated using age-period and cause-specific cancer incidence rates for the WA female population in 5-year periods from 1982 to 2005, provided by the WA Cancer Registry. For the period 1960–1981 the population age and cause-specific cancer incidence rates for 1982–1984 were used to estimate expected cancers as period specific rates were unavailable. However, cancers diagnosed before 1982 were not included in the SIR analysis. For mesotheliomas, age and period specific incidence rates for the WA female population in 5-year periods from 1982 to 2005 were used to calculate expected numbers. For mesotheliomas diagnosed prior to 1982 incidence rates for the period 1982–1984 were used as period specific rates for 1960–1981 were not available. The usual method for calculating expected cancers would lead to a probable overestimate of risk,[2] given that 22% of the women were lost to follow up and the nearly complete ascertainment of cancers in WA. Therefore two methods were used to derive expected cancers, to show minimum and maximum estimates of effect, based on differing censoring dates. The first method assumed that all women who were not diagnosed with a cancer, not known to be dead, and not known to have migrated were cancer-free at the end of 2004 or, if they were residents of other Australian states, they were cancer-free until their respective state end of follow up date. This method tends to overestimate the person-years at risk and therefore provides a minimum estimate for SIR. The second method censored women at their date last known to be alive if they were not diagnosed with a cancer, known to be dead or to have migrated. This method tends to underestimate person-years at risk and therefore gives an upper estimate of SIR. Both methods censored women at age 85 years if they were not known to have a cancer or to have died before that age.

Mesothelioma incidence rates were derived in 10 year periods of time since first exposed to asbestos at Wittenoom and for each 5 year period from 1960, by dividing the number of cases in each time span by the number of person-years at risk in the same time span and multiplied by 100,000. Those women who were lost to follow up were censored at their date last known to be alive.

Exposure-response relationships were examined using a nested case-control analysis. Cases were those women who were diagnosed with a cancer of interest during the study period. Controls were all those not known to have been diagnosed with the same cancer by the year of diagnosis of the case and who were the same age as the case, in 5 year age-bands. Conditional logistic regression related asbestos exposure to cancer outcome. Asbestos exposure measurements were not normally distributed and so were transformed to their natural log. All analysis was undertaken using Stata 9.0.[26]

Results

Descriptive results

There were 437 incident cancers in 387 women among the Wittenoom women between 1960 and 2005. The age at diagnosis ranged from 10 to 99 years. Cases were more likely to arrive at Wittenoom in the 1940s and 1950s, and to be older on their arrival than women who remained cancer free although their duration of residence at Wittenoom was not significantly different (Table II). There was no difference in duration of residence between case and non cases, with 45% of all women staying at Wittenoom for 1 year or less. Twenty percent of former ABA workers compared with 12% of former residents were diagnosed with a cancer. Cases had a greater intensity of asbestos exposure and a greater cumulative asbestos exposure than non cases. Among former residents, 72% of those who developed a subsequent cancer had lived with an ABA asbestos miner or miller and 35% reported washing the clothes of an ABA worker.

Incidence of cancers

For all the Wittenoom women combined, the incidence of all cancers, malignant mesothelioma and cancer of the lung, trachea and bronchus was greater than that of the WA female population irrespective of which censoring method was used. The incidence of mesothelioma was 55–77 times greater than in the WA female population. The SIR for lung cancer was 80% to 254% higher among the Wittenoom women than women in the WA population. Regarding smoking status we have limited information. For all women we have smoking information on 59% of whom 53% reported being an ever smoker. Applying Axelson's adjustment to our data, we estimate that the lung cancer SIR is raised by a factor between 1.4 and 1.5 due to confounding by smoking.[27,28] Therefore SIR1 might be adjusted down to 1.27 and SIR2 to 1.75.

Among former ABA workers, the incidence of mesothelioma and lung cancer was raised, compared to the WA female population irrespective of which censoring method was used (Table III). Thirty four percent of former workers responded to a smoking questionnaire in 1979 and 49% reported currently smoking. Applying Axelson's adjustment attenuated the lung cancer SIR1 to 1.92 and SIR2 to 2.91. All cancers incidence was increased with SIR2 (women lost to follow up censored at their date last known to be alive). Cervical cancer was between 90% and 250% greater among the Wittenoom workers than the WA female population, but this was not statistically significant.

Among former residents of Wittenoom, the incidence of mesothelioma, all cancers and lung cancer was increased compared to the WA female population, irrespective of which censoring

TABLE II – RESIDENTIAL AND ASBESTOS EXPOSURE CHARACTERISTICS FOR ALL CANCER CASES AND NON CASES AMONG THE WOMEN FROM WITTENOOM

	Cases *N* (%)	Non cases *N* (%)	Total *N* (%)	*p*-value
Year of arrival at Wittenoom				
1940s	22 (6)	95 (4)	117 (4)	
1950s	184 (48)	907 (35)	1,091 (37)	
1960s	147 (38)	1,174 (45)	1,321 (45)	
1970s	31 (8)	382 (15)	413 (14)	
Unknown	3 (1)	23 (1)	26 (1)	
Total	387	2,581	2,968	$p < 0.001$
Age of arrival at Wittenoom				
<15 years	65 (17)	1,157 (45)	1,222 (41)	
15–39 years	252 (65)	1,164 (45)	1,416 (48)	
40+ years	67 (17)	227 (9)	294 (10)	
Unknown	3 (1)	33 (1)	36 (1)	
Total	387	2,581	2,968	$p < 0.001$
Duration of residence at Wittenoom				
Less than 1 year	175 (45)	1,162 (45)	1,337 (45)	
One to less than 3 years	91 (24)	691 (27)	782 (26)	
Three to less than 5 years	62 (16)	390 (15)	452 (15)	
Five years or more	57 (15)	310 (12)	367 (12)	
Unknown	2 (1)	28 (1)	30 (1)	
Total	387	2,581	2,968	$p = 0.328$
Average Intensity of exposure (f/ml)				
<2 f/ml	128 (33)	908 (36)	1,036 (35)	
2 to <5 f/ml	235 (61)	1,572 (62)	1,807 (62)	
5 to <10 f/ml	15 (4)	51 (2)	66 (2)	
10+ f/ml	6 (2)	21 (1)	27 (1)	
Unknown	3 (0)	29 (1)	32 (1)	
Total	387	2,581	2,938	$p = 0.049$
Cumulative exposure (f/ml years)				
<10 f/ml years	302 (78)	2,161 (85)	2,463 (84)	
10 to <20 f/ml years	54 (14)	257 (10)	311 (11)	
20 to <30 f/ml years	16 (4)	82 (3)	98 (3)	
30 to <40 f/ml years	8 (2)	31 (1)	39 (1)	
40+ f/ml years	5 (1)	21 (1)	26 (1)	
Unknown	2 (0)	29 (1)	31 (1)	
Total	387	2,581	2,968	$p = 0.038$
Worker	84 (20)	332 (80)	416	
Resident	303 (12)	2,249 (88)	2,552	$p < 0.001$
Live with ABA worker[1]	219 (72)	1,462 (65)	1,681 (66)	$p = 0.012$
Wash clothes of ABA worker[1]	107 (35)	459 (20)	566 (22)	$p < 0.001$

[1]Residents only.

method was used. Sixty percent of residents returned a questionnaire in the early 1990s and 26% reported currently smoking compared with 20% in the Australian female population. Applying Axelson's adjustment attenuated the lung cancer SIR1 to 1.11 and SIR2 to 1.47. Former workers had greater SIRs for mesothelioma, all cancers, lung cancer and cervical cancer compared to former residents.

Including those cancers ($n = 36$) diagnosed before 1982 and their respective person years at risk attenuated SIR1 to 0.96 (95%CI 0.87–1.06) and SIR2 to 1.23 (95%CI 1.11–1.36) for all cancers among all women (not shown). For the period 1960 to 1981 SIR1 was 2.50 (95%CI 0.52–7.31) and SIR2 was 3.25 (95%CI 0.67–9.53) for ovarian cancer among former workers. Inclusion of these 3 ovarian cases increased the SIR1 for the period 1960–2005 to 1.25 (95%CI 0.34–3.21) and SIR2 to 1.73 (95%CI 0.47–4.43). All other SIRs were moderately attenuated if the cases diagnosed prior to 1982 were included.

Mesothelioma among workers and residents

There were 47 cases of malignant mesothelioma (46 pleural). The first woman was diagnosed in 1975 and the youngest was aged 27.5 years. The proportion of ABA workers with mesothelioma was double that of the residents 2.5% and 1% respectively. There was no significant difference in age of arrival ($p = 0.069$) at Wittenoom for workers or residents with mesothelioma or year of arrival ($p = 0.168$) although residents stayed longer at Wittenoom than workers ($p = 0.003$). The median length of stay at Wittenoom for a worker was 2.2 years (IQR 0.4–2.7 years) and for a resident 4.5 years (IQR1.9–6.4 years). Therefore cumulative asbestos exposure was significantly greater for residents, median 12.2 f/ml years (IQR 5.8–25.5 f/ml years), than for workers, median 3.6 f/ml years (IQR 0.89–14.4 f/ml years). There was no difference in the intensity of asbestos exposure between workers and residents who subsequently developed mesothelioma; workers median 1.7 f/ml (IQR 1.4–5.3 f/ml), compared with residents 3.1 f/ml (IQR 2.1–4.2 f/ml), although the exposure measurements were derived differently for workers and residents (see Methods section). The first case of mesothelioma in a worker occurred 24.6 years after first exposure to asbestos (e.g., arrival date in Wittenoom) and 23.5 years in a resident. The time from first exposure to onset of mesothelioma ranged from 23.5 years to 51.8 years (median 38 years) and was shorter for workers (median 34.1 years, IQR 27.1–38.6 years) than for residents (median 39.3 years, IQR 34.7–43.6 years). The incidence rate among workers appears to have peaked 30–39 years after first exposure, with only one case occurring more than 40 years after first exposure. For residents, peak incidence occurred after more than 40 years. At every 5-year period after 1975 the incidence rate was greater among workers than residents and appears to be still increasing (Table IV). The doubling of mesothelioma cases among the former workers and their shorter latency period compared to the residents suggests that the asbestos exposure measurement for the workers underestimates their actual exposure.

TABLE III – STANDARDIZED INCIDENCE RATIOS FOR MALIGNANT MESOTHELIOMA, 1960–2005 AND SPECIFIC CANCERS 1982–2005 FOR WOMEN FROM WITTENOOM

Cancer	ICDO-2 Code	Observed	SIR1[1] (95%CI)	SIR2[2] (95%CI)
All women				
1960–2005				
Malignant mesothelioma	C384, C481–C482 and M9050–M9055	47	55.9 (41.1–74.4)	77.0 (56.6–102.5)
1982–2005				
All cancers[3]	C000–C809	330	1.12 (1.00–1.25)	1.51 (1.35–1.68)
Lung, trachea and bronchus	C330–C349	45	1.84 (1.30–2.38)	2.54 (1.80–3.29)
Breast cancer	C500–C509	82	0.89 (0.69–1.08)	1.19 (0.93–1.44)
Ovarian cancer	C560–C569	10	0.98 (0.37–1.58)	1.30 (0.49–2.11)
Cervical cancer	C530–C539	12	1.13 (0.49–1.77)	1.42 (0.62–2.23)
Corpus uterine cancer	C540–C549	12	0.98 (0.43–1.54)	1.32 (0.58–2.07)
Colorectal cancer	C180–C209	31	0.76 (0.49–1.03)	1.03 (0.67–1.40)
Workers				
1960–2005				
Malignant mesothelioma	C384, C481–C482 and M9050–M9055	11	64.7 (32.3–116)	82.7 (41.3–148)
1982–2005				
All cancers[3]	C000–C809	65	1.13 (0.86–1.41)	1.66 (1.26–2.06)
Lung, trachea and bronchus	C330–C349	15	2.88 (1.42–4.34)	4.36 (2.15–6.57)
Breast cancer	C500–C509	13	0.78 (0.36–1.21)	1.11 (0.51–1.72)
Ovarian cancer	C560–C569	1	0.50 (0.01–2.80)	0.72 (0.02–4.01)
Cervical cancer	C530–C539	3	1.89 (0.39–5.51)	2.48 (0.51–7.25)
Corpus uterine cancer	C540–C549	2	0.81 (0.10–2.91)	1.16 (0.14–4.20)
Colorectal cancer	C180–C209	6	0.68 (0.14–1.22)	1.04 (0.21–1.87)
Residents				
1960–2005				
Malignant mesothelioma	C384, C481–C482 and M9050–M9055	36	52.9 (37.1–73.3)	76.6 (53.6–106)
1982–2005				
All cancers[3]	C000–C809	265	1.12 (0.99–1.26)	1.48 (1.30–1.66)
Lung, trachea and bronchus	C330–C349	30	1.57 (1.01–2.13)	2.09 (1.34–2.84)
Breast cancer	C500–C509	69	0.91 (0.69–1.12)	1.21 (0.92–1.49)
Ovarian cancer	C560–C569	9	1.11 (0.39–1.84)	1.43 (0.50–2.37)
Cervical cancer	C530–C539	9	1.01 (0.35–1.67)	1.23 (0.43–2.03)
Corpus uterine cancer	C540–C549	11	1.13 (0.46–1.79)	1.48 (0.61–2.36)
Colorectal cancer	C180–C209	25	0.78 (0.48–1.09)	1.03 (0.63–1.44)

[1]Minimum estimate—censored at earliest of: date of diagnosis, date of death, date aged 85 or end-date of state cancer registry follow-up.–[2]Maximum estimate censored at earliest of: date of diagnosis, date of death, date aged 85 or date last known to be alive.–[3]For women with multiple cancers—first diagnosed cancer included in this analysis.

TABLE IV – MALIGNANT MESOTHELIOMA INCIDENCE RATE, PER 100,000 PERSON YEARS, BY TIME SINCE FIRST EXPOSURE AND YEAR OF DIAGNOSIS AMONG THE WITTENOOM WOMEN

Time since first exposure	All women		Workers		Residents	
	Observed	Rate[1] (95% CI)	Observed	Rate[1] (95% CI)	Observed	Rate[1] (95% CI)
0–19 years	0	–	–	–	0	–
20–29 years	8	35 (17–70)	3	101 (33–314)	5	25 (10–60)
30–39 years	20	119 (77–184)	7	304 (145–637)	13	90 (52–154)
40+ years	19	256 (163–401)	1	114 (16–811)	18	275 (173–436)
Year of diagnosis						
1960–64	0	–	0	–	0	–
1965–69	0	–	0	–	0	–
1970–74	0	–	0	–	0	–
1975–79	3	24 (8–76)	1	63 (9–446)	2	19 (5–75)
1980–84	4	33 (12–88)	1	67 (9–476)	3	28 (9–88)
1985–89	5	42 (18–102)	1	71 (10–503)	4	39 (14–103)
1990–94	14	127 (75–214)	3	236 (76–733)	11	112 (62–203)
1995–99	8	84 (42–168)	1	94 (13–664)	7	83 (39–174)
2000–05	13	193 (112–332)	4	542 (203–1444)	9	150 (78–288)

[1]Women lost to follow up censored at date last known to be alive.

Exposure-response relationships—mesothelioma

The risk of mesothelioma stratified by worker and resident status and adjusted for time since first exposure and age, significantly increased with every unit increase in log fiber ml years (Table V). Among workers the risk increased 75% for every unit of log fiber ml year. For residents this risk was almost 3-fold. The risk of mesothelioma increased for those residents who had washed the clothes of OR = 1.68 (95%CI 0.66–4.29) or lived with OR = 2.57 (95%CI 0.96–6.84) an ABA asbestos worker (not shown).

Lung cancer

The risk of lung cancer stratified by worker and resident status and adjusted for time since first exposure and age increased with every unit of log fiber per ml years but not significantly. The risk of lung cancer increased in those residents who lived with an ABA worker OR = 2.61 (95%CI 1.09–6.21). There was no increase in lung cancer risk among those residents who washed the clothes of an ABA worker, OR = 1.14 (95%CI 0.46–2.81). Among the 55 cases of lung cancer, 14 were adenocarcinomas, 7

TABLE V – EXPOSURE-RESPONSE RELATIONSHIPS[1] BETWEEN CUMULATIVE ASBESTOS EXPOSURE, MALIGNANT MESOTHELIOMA ADJUSTED FOR AGE AND TIME SINCE FIRST EXPOSURE, AMONG ALL WITTENOOM WOMEN AND AMONG FORMER WORKERS AND RESIDENTS SEPARATELY

Cancer	Odds ratio (95%CI)	*p*-value
Workers		
Malignant mesothelioma 11 cases min 8 max 297 non cases		
Cumulative exposure log(f/ml years)	1.77 (1.11–2.82)	0.017
Cancer of the lung, trachea and bronchus 18 cases, min 3 max 283 non cases		
Cumulative exposure log(f/ml years)	1.25 (0.90–1.72)	0.179
Residents		
Malignant mesothelioma 36 cases, min 68 max 1,632 non cases		
Cumulative exposure log(f/ml years)	2.73 (1.94–3.82)	<0.001
Cancer of the lung, trachea and bronchus 37 cases, min 44 max 1,563 non cases		
Cumulative exposure log(f/ml years)	1.09 (0.83–1.41)	0.543

[1]Women lost to follow up censored at date last known to be alive.

squamous cell, 8 small cell, 3 large cell and 23 of indeterminate histology. Further examination of the adenocarcinomas showed non-significant increases in risk with quantitative measures of the intensity of asbestos exposure (f/ml) (OR = 1.87 95%CI 0.82–4.27), the length of stay at Wittenoom (OR = 1.07 95%CI 0.98–1.16) and cumulative asbestos exposure (f/ml years) (OR = 1.43 95%CI 0.92–2.24).

Discussion

The impact of exposure to blue asbestos on subsequent cancer incidence among the women of Wittenoom has been cruel. Although the time they spent at Wittenoom was short (median 1.3 years), 47 women developed mesothelioma. A further 55 women developed lung cancer. Compared with the Western Australian female population Wittenoom women had a significantly greater risk of all cancers, cancer of the lung, trachea and bronchus and malignant mesothelioma. There was a significant exposure-response relationship between asbestos exposure and malignant mesothelioma for both workers and residents, but not lung cancer.

Our findings are similar to those few studies that have looked at mortality outcomes in women exposed to asbestos in their workplace. World War II gas mask workers subsequently experienced high mortality from mesothelioma SMR = 111.5(95%CI 84.5–146.8), respiratory cancer SMR = 2.5(95%CI 1.7–3.5) and carcinomatosis SMR = 3.2 (95%CI 1.8–5.4) with evidence of increased risk related to duration of exposure.[8] Among a second group of gas mask workers in England rates were also increased for cancer of the lung and pleura SMR = 2.41 (95%CI 1.35–3.97) and cancer of the ovary SMR = 2.75 (95%CI 1.42–4.81) but exposure-response was not examined.[9]

Following up women for decades in cohort studies is difficult given the frequency of name changes due to marriage and divorce and the extent of migration over the period. This may explain why women are often excluded from such studies. We have used various means to reduce our loss to follow up; tracing on the electoral roll (voting is compulsory in Australia and the electoral roll is carefully maintained), searches of the electronic white pages and participation in a cancer prevention program.[16] Italian migrants to Wittenoom who subsequently returned to Italy have been traced in Italy, but this information relates to male ABA workers and not their wives or families.[29] Twenty two percent of the women were defined as lost to follow up most from the time they left Wittenoom. The difficulty maintaining follow-up on this cohort of women may have led to an underestimation of asbestos-related cancers.

We had only limited information on tobacco smoking in this cohort. Applying Axelson's adjustment to our lung cancer SIRs reduced them substantially, although for women workers the risk remains double that of the WA female population, and for all women there remains a 27% increase (SIR1). The high rates of smoking in this cohort probably increased the risk for all cancers reported among this cohort and may have increased cervical cancers among the women workers.[30] There is no association between tobacco smoking and risk of mesothelioma.

The mesothelioma incidence rates reported here (35–256 per 100,000 person-years) are among the highest for any known group of women in the world. The age standardized rate for Western Australian women in 2005 was 0.9 per 100,000.[31] Internationally; among women with environmental exposure in Casale Monferrato Italy, incidence rates of 2.3 to 5.1 per 100,000 person years were reported,[32] whilst Camus *et al*., report incidence rates among women of 67.5 per million person years and 13.7 per million person years in the Thetford and Asbestos areas respectively of Quebec for the period 1970–1989.[33] For the period 1979–1990 incidence rates of 95.9 per million were reported for women in Manville, NJ, where the largest asbestos manufacturing plant in the United States was located.[34] The women at Wittenoom were exposed exclusively to crocidolite, whereas the women in the other studies were exposed primarily to chrysotile. The mesothelioma mortality rate reported for former gas mask workers exposed mostly to crocidolite for the period 1956–2003 was 138.1 per 100,000 person years,[8] which is between the rates for the Wittenoom residents and the ABA workers.

The duration of residence at Wittenoom was short. Forty five percent of women, cases and non cases, lived at Wittenoom for one year or less. Among those women who subsequently developed mesothelioma the median duration of residence was also short at 2 years for workers and 4.5 years for residents. Other asbestos exposed cohorts with high mortality and cancer incidence report short durations of exposure. Among female British gas mask workers (exposed to Wittenoom crocidolite) the duration of employment was also short with 35% employed for less than 6 months and only 4% employed for longer than 5 years. Those women employed for less than 1 year showed excess mortality from all cancers and lung cancers after 33 years of follow up.[7] Similarly for the largely male ABA miners and millers the median period of employment was brief at 4 months.[2] Possibly a short but intense exposure to asbestos is more harmful than a longer exposure at lower levels.

This study found that ABA workers had a greater risk for mesothelioma and lung cancer than residents. The exposure measurements for the workers and residents were derived using different types of data, which could be one possible explanation for this difference. Workers exposures were derived from one comprehensive dust survey undertaken in 1966 across various workplaces in the mine and mill.[20] Exposures for the residents were derived from this comprehensive survey as well as various other studies using personal monitors over the 1970s to early 1990s.[10] Using results from several surveys may have increased the possibility of measurement error, although it may also have allowed better measurement as more data was available therefore reducing the amount of interpolation between surveys over time. Any measurement error or bias is likely to be non differential because it would not differ with disease status. The effect of nondifferential misclassification on the asbestos mesothelioma association would be to attenuate

the results towards the null and so lessen the association shown for residents. Further, the asbestos exposure measurements are likely to be underestimates for the former worker women. Most women did not work in the mine or mill or even on the site of operations, but in the town. However where women did work onsite they tended to work in the company office which was located downstream of the mill. The fly screens in the office were covered with dust and words could be written on the fibers that settled on the desks. Women workers in the office were not offered the annual chest X-rays given to the miners and millers.[36] Those who worked in the hotel and shop in town were also in contact with workers who would enter in their dusty work clothes.

Examination of differences between women workers and residents with mesothelioma revealed no difference in their age of arrival at Wittenoom or their year of arrival. Residents tended to live at Wittenoom longer than workers. Of the 11 workers who developed mesothelioma only one had worked in the bagging room in the mill (probably the "dirtiest" area in terms of asbestos dust in Wittenoom); three others had worked as Clerks in the office, which was located within 1 km of the mill[36]; one worked in the Canteen (also near the mill), two worked as assistants in the Company shop in the town and two worked as Barmaids in the hotel in the town, and we had missing information for 3 women. Worker women may have also have had domestic exposure (most women were at Wittenoom with their husbands who were employed in the mine or mill) and we know that some of the Wittenoom women laundered other ABA workers' clothes (in an attempt to increase savings so that they could leave Wittenoom sooner).[37] Unfortunately we do not have information on domestic exposure among the female workers. We found that domestic exposure tended to increase the risk of malignant mesothelioma in the residents. Chrysotile samples taken from inside asbestos miners and millers houses in the United States ranged from a minimum of 50–100 ng/m^3 to a maximum between 2,000–5,000 ng/m^3.[38] If these figures are comparable to the levels that Wittenoom women were exposed to in their houses then it is not a large addition to their already high exposure obtained from their workplaces. A study among the wives of asbestos cement factory workers in Casale Monferrato, Italy reported excess mortality from cancer of the pleura SMR = 792 (95% CI 216–2,029) following only domestic exposure to asbestos. These women lived in the same township as the asbestos cement factory (as did the Wittenoom women) so it was not possible to disentangle the environmental and domestic exposure.[39] A meta-analysis examining domestic and neighborhood exposure and risk of pleural mesothelioma reported an RR = 8.1 (95%CI 5.3–12) for domestic exposure and RR = 7.0 (95%CI 4.7–11) for neighborhood exposure.[40]

This study found that the latency period between exposure to blue asbestos at Wittenoom and diagnosis with malignant mesothelioma in ABA workers was significantly shorter than that in residents and consequently the incidence rate in workers appears to have peaked earlier than that of the residents. We have earlier reported a longer latency period in Wittenoom residents compared with the Wittenoom (male) ABA workers.[15] A longer latency period is consistent with the lower risk for mesothelioma experienced by residents compared to workers. Metintas *et al*., suggested that a higher level of asbestos exposure (as seen in occupational *vs*. environmental exposure) might shorten the latency time.[41]

The pattern of mesothelioma incidence rates in the women workers shows a different pattern to that of the male ABA workers. The first cases of mesothelioma among the male workers developed between 10 and 19 years since first exposure whereas for women this was 20–29 years. On the other hand the mortality rate for the male workers was of a similar magnitude to the women's incidence rate for the periods 20–29 years (115 per 100,000 person years) and 30–39 years (281 per 100,000 person years) since first exposure.[24] The rate among male workers continued to increase in those with 40 or more years since first exposure (364 per 100,000 person years) unlike the women worker's rate that appeared to decline among those with 40 or more years since first exposure. The median estimated cumulative exposure for male workers was 6.0 f/ml years compared to 0.5 f /ml years for women workers.[2] More than 600 women residents came to Wittenoom after the mine and mill closed in December 1966, when exposure levels in the town were substantially lower than during the period of mill operation. To the end of 2005 one of these has subsequently developed mesothelioma.

To date there have been no new cases of mesothelioma among women who were first exposed to asbestos more than 52 years ago. However this may change as the median time since first exposure was 37 years (IQR 27–44 years) as at the end of 2005. Among female gas mask workers exposed to crocidolite no cases of mesothelioma arose more than 51 years after first exposure[8] and among workers at the "Eternit" asbestos cement factor in Casale Monferrato, Italy latency of more than 50 years was associated with a reduced risk of mesothelioma, although with wide confidence intervals.[42] Similarly Musk *et al*., found that the rate of mesothelioma appeared to level off after 50 years since first exposure in the Wittenoom workers.[43] This suggests that crocidolite fibers are eventually cleared from the mesothelium. Fiber clearance has been observed experiments in rats[44] and baboons.[45] Lung fiber counts at postmortem from female gas mask workers exposed to a high intensity but relatively short duration of crocidolite asbestos suggested a rate of clearance of ~15% per annum.[46] Longer follow up is necessary to determine if the risk of mesothelioma levels off or even decreases after 50 years have passed since first exposed to asbestos.

Conclusion

Forty years after the asbestos mine and mill at Wittenoom were closed, there is a high toll from cancer among the former female residents of the town and company workers. Women from Wittenoom have greater rates of mesothelioma and possibly lung cancer than women in the WA population. There was a significant exposure-response relationship with mesothelioma but not lung cancer. There were fewer cases of mesothelioma, a different pattern of incidence, lower asbestos exposure and no demonstrated exposure-response relationship for lung cancer among the women compared to the largely male ABA workers. These differences emphasize the importance of examining women and men separately, where possible, with regards to disease outcome.

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